295. (New) A method for producing oil with an altered fatty acid profile comprising extracting said oil with an altered fatty acid profile from the microbial cell culture produced according to the method of claim 294.

296. (New) A microbial cell culture with an altered fatty acid profile produced according to the method of claim 294. --

REMARKS

The Unity of Invention Objection

The Office Action of June 28, 2002 stated that claims 189-214 and 215-284 were drawn to two independent methods which do not relate to a single inventive concept under PCT Rule 13.1.

Applicants traverse the withdrawal of claims 189-214 from consideration, and request reconsideration by the Examiner in light of the following. The single inventive concept to which all the claims relate is a product that is a microbial cell culture with an altered fatty acid profile by virtue of expression of a sufficient amount of a Δ6-desaturase. Claims 189-214 relate to a method for production of this product, and claims 215-284 relate to a method of use of this product to produce an oil with an altered fatty acid profile.

MPEP 1850.C. (p. 1800-62) states:

> "The method for determining unity of invention under PCT Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:
>
> (A) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product. ...
>
> The words "specially adapted" are not intended to imply that the product could not also be manufactured by a different process." (emphasis added)

Here, applicants have presented claims for a method of making a given product, and claims for a method for use of that product, which have not previously been restricted from each

other. The MPEP states that these sets of claims share unity of invention under PCT rules, and further allow for the inclusion of claims to the product itself. Applicants have therefore added claims to a microbial cell culture having an altered fatty acid profile by virtue of expression of a sufficient amount of a Δ6-desaturase.

The Office Action further stated that the nucleic acid sequence of SEQ ID NO: 1 was known at the time of the invention. However, the nucleic acid sequence of SEQ ID NO: 1 was not known at the time this invention was made, the nucleic acid represented in SEQ ID NO: 1 has previously been found novel and nonobvious, the patent for which shares priority with this application.

In accordance with MPEP 1850.C., Applicants respectfully request that claims 189-214 be considered along with claims 215-284 and new claims 285-296, as they share unity of invention as defined by the MPEP.

The Objection to the Specification

Antecedent basis. The Office Action stated that the specification as lacking proper antecedent basis for certain subject matter: (i) "deletion mutant of the nucleic acid sequence of SEQ ID NO: 1" in claims 235 and 245; (ii) "at least 60% homology to SEQ ID NO: 2" in claim 265; and (iii) "nucleic acid that hybridizes to the complement of the sequence depicted in SEQ ID NO: 1" in claim 275. This objection is traversed.

The application need not provide an *ipsis verbis* description for the claims, only such description as would reasonably convey that Applicants were in possession of the claimed invention at the time the application was filed. MPEP 2163. All parts of the application can contribute to the description, including the figures, specific embodiments, sequence listings, and the original claims.

The application states that "[n]ovel compositions and methods are provided for preparation of polyunsaturated long chain fatty acids. ... The methods involve growing a host microorganism or animal expressing an introduced gene or genes encoding at least one desaturase" (page 4 lines 19-24).

Support for claims involving a deletion mutant of the Δ6-desaturase can be found in the

application as set forth in the prior amendment. Extensive discussion of deletion mutants of the desaturases disclosed in the application is provided at page 21 lines 14-32, and is accompanied with disclosure of insertion mutants, point mutants, cassette mutagenesis, chemical mutants. "All such mutant proteins and nucleotide sequences encoding them are within the scope of the present invention" (page 22, lines 9-10).

Polypeptides having at least 60% homology to the *M. alpina* Δ6-desaturase are described at page 19, lines 22-28. Extensive description of methods of determining homology are provided from page 19 line 25 through page 20 line 17. Support for new claims 291-296 can also be found at those passages.

Nucleic acids that hybridize to the disclosed desaturase nucleic acids, including SEQ ID NO:1, are described for example at page 5 lines 25-26, page 9 lines 5-11, page 17 line 30 through page 18 line 14, and page 21 lines 9-11.

As all the claim terms objected to find antecedent support in the specification as set forth above, no new subject matter was added in the last amendment. Withdrawal of the objection is requested.

Trademarks. The specification has been amended extensively above to address the trademark issues identified in the Office Action.

The objection to claims 215-284 as dependent on nonelected subject matter

Claims 215-284 were objected to as dependent on nonelected subject matter. This objection is traversed. As set forth above, claims 215-284 are dependent on claims with which they are properly grouped. MPEP 1850.C. states the PCT Rule 13 shall be construed as permitting such a combination of claims. Therefore claims 215-284 are dependent on elected subject matter. Withdrawal of the objection is requested.

The Double Patenting Rejections

A terminal disclaimer is filed herewith disclaiming the term of any patent resulting from this application that would extend beyond the term of the latest expiring of U.S. Pats. Nos. 6,136,574, 6,075,183 and 5,968,809. The double patenting rejections are therefore moot.

The enablement rejection

Claims 225-254 and 265-284 were rejected as lacking enablement. This rejection is traversed.

The Office Action acknowledged that the specification provides guidance and teaching regarding the *M. alpina* Δ6 and Δ12-desaturases "and their use in obtaining unsaturated fatty acid from a culture of microorganism (see examples 1-8) and isolation and determining the amount of each unsaturated fatty acid in a lipid fraction" (sentence bridging pages 4-5). The Office Action further stated that molecular biological techniques and genetic manipulation and the skill of the artisan are well developed. The Office Action also stated that "[t]he amount of experimentation to identify a nucleic acid encoding a polypeptide having 60% sequence homology to SEQ ID NO: 2 or a nucleic acid having 50% sequence homology to SEQ ID NO: 1 and having the desaturase activity of SEQ ID NO: 2 is enormous." The Office Action also objected to the recitation of any nucleic acid that "hybridizes under any set of conditions to or deletion mutation of SEQ ID NO: 1" as overbroad (page 4, last paragraph).

Identification of whether or not a protein or nucleic acid has homology to a disclosed sequence is routine in the art, and methods for accomplishing this are described in the application from page 19 line 25 through page 20 line 17. Extensive teachings regarding deletions, insertions, substitutions, and methods of mutating isolated sequences are provided in the specification at page 21 line 14 through page 22 line 21.

Nevertheless, claims 193 and 208, on which claims 225 and 265 depend, have been amended to recite at least 80% homology to SEQ ID NO: 1 or SEQ ID NO: 2, respectively. The PTO has found claims of such scope enabled and allowable, including by SPE Prouty in copending case S.N. 09/377,452 involving Δ5-desaturase proteins from *M. alpina*.

Deletion analysis of a given gene is routine in the art, and the results are entirely predictable. The amino acid residues from which the deleted residues can be selected are set forth in SEQ ID NO: 2. Techniques for deleting given residues were known in the art more than ten years prior to the priority date of this invention and are described in the specification at page 21 lines 14-32. Such systematic deletion analysis was routine at the time of invention. Kits were available for accomplishing this. Through routine deletion analysis as taught in the specification,

residues which can be deleted while still allowing for enzymatic function are readily and reliably identified. No undue experimentation is necessary. Furthermore, the PTO has also found claims of such scope enabled and allowable in copending case S.N. 09/377,452.

Claim 214, on which claim 275 depends, has been amended to recite that the recombinant nucleic acid "hybridizes to the complement of the sequence depicted in SEQ ID NO: 1 under hybridization conditions suitable for sequencing said complement." Primer-based sequencing is one embodiment of a nucleic acid hybridizing to the complement of SEQ ID NO: 1. Sequencing conditions are well known in the art and can be readily determined by one of skill in the art. Primer-based sequencing is described in the application at page 18 lines 16-28, and working examples of sequencing are given at page 47 lines 3-7 and lines 17-22 and in Examples 3, 4, 10 and 11, and the results are shown in the figures and the sequence listings. No undue experimentation is necessary for one of skill in the art to determine hybridization conditions suitable for sequencing the complement of SEQ ID NO: 1. Furthermore, such sequencing conditions are specific and would not result in the random hybridization postulated in the Office Action.

Accordingly, the claims are asserted to be enabled and allowable. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

The rejections under 35 U.S.C. §112, second paragraph

Claims 215-284 were rejected as indefinite on various grounds. These rejections are traversed.

The Office Action stated that (a) "the phrase 'microbial cell produced according to the method of claim' ... is render the claim indefinite," further stating that none of the methods produce a transformed host cell. This phrase appears to have been misinterpreted. The microbial cell, containing a Δ6-desaturase, is produced by culturing, as stated in the claims on which the referenced claims depend. The method claims do not involve any transformation steps. The claims have been amended to clarify that what is produced is a culture of cells having an altered fatty acid profile (as claimed) by virtue of expression of a Δ6-desaturase.

The Office Action stated that (b) "the phrase 'altering fatty acid profile' ... is render the

claim indefinite." The Office Action stated that one of ordinary skill in the art would not know in which way the fatty acid profile is altered. The Office Action acknowledges, however, that "[t]he specification provides guidance and examples in the form of an assay to isolate and characterize the nucleic acid encoding [desaturases] and their use in obtaining unsaturated fatty acid from a culture of microorganism (see examples 1-8) and isolation and determining the amount of each unsaturated fatty acid in a lipid fraction." Office Action, sentence bridging pages 4-5.

The Office Action thus acknowledges that one of skill in the art can culture a microorganism containing a desaturase disclosed in the specification to produce unsaturated fatty acids, and can isolate and determine the amount of each unsaturated fatty acid in a lipid fraction (a fatty acid profile). Nothing further is needed to determine whether the fatty acid profile has been altered. The phrase therefore appears clear to the Examiner, and is clear to one of skill in the art. One of skill in the art can determine a fatty acid profile following the specifications teachings, and can determine if that profile has been altered in a cell culture expressing a Δ6-desaturase by running a simple control experiment.

MPEP 2173.01 states:

> A fundamental principle contained in 35 U.S.C. 112, second paragraph is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose so long as the terms are not used in ways that are contrary to accepted meanings in the art. Applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. As noted by the court in *In re Swinehart*, 439 F.2d 210, 160 USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought. (Emphasis added)

The claims by their terms cover methods in which any alteration in fatty acid profile is made as a result of culturing a microorganism expressing a recombinant Δ6-desaturase. Applicants have provided working examples of such methods. One of skill in the art can determine whether an alteration in fatty acid profile has occurred, as acknowledged in the Office Action. The metes and bounds of the claim are thus clear. The Office Action's primary objection seems to be with the breadth of the claim, having difficulty with not knowing in which

way the profile is altered. However, "[b]readth of a claim is not to be equated with indefiniteness." MPEP 2173.04.

Furthermore, as one of skill in the art would recognize, the language proposed in the Office Action ("an increased amount stearidonic acid") is unnecessarily limiting and inaccurate in many embodiments. One of skill in the art would recognize that stearidonic acid (SDA) is only one product which can be produced by the immediate action of a Δ6-desaturase, and only in a cell having the appropriate precursor thereto, α-linolenic acid (ALA). A Δ6-desaturase can also be used to produce γ-linolenic acid directly, or a wide range of subsequent metabolic products including the fatty acids shown in Fig. 2. Even in a cell which provides or is supplemented with ALA, stearidonic acid would only accumulate if no subsequent metabolic processes were performed on it in the host cell, or if an enzyme acting on stearidonic acid in a metabolic pathway (for example the elongase shown in Fig. 2, or an enzyme converting SDA into acyl glycerols, sulfolipids, phospholipids, etc.) were rate-limiting. Indeed, many embodiments taught by Applicants of producing recombinant cells involve manipulating the levels of multiple enzymes in fatty acid metabolic pathways to alter the fatty acid profile in desirable ways (see, for example, page 13 line 4 through page 14 line 25, and page 16 line 24 through page 17 line 15). One of skill in the art would also recognize that expression of the Δ6-desaturase could also alter the profile by decreasing the amount of a precursor to stearidonic acid or other Δ6-desaturase substrate by following Applicants' teachings.

The language "altering the fatty acid profile" accurately reflects the result of following this disclosed method. Applicants are entitled to the full range of protection for any alteration in fatty acid profile which occurs as a result of any process performing the method steps taught in the application.

The Office Action objects in part (c) that the claims are incomplete by the omission of asserted essential steps, including (a) culturing, (b) inducing, and (c) isolating the oil. Again, for (a) here, as in (a) above, this appears to be a misinterpretation of the claims. In order to clarify this, the claims have been amended to clarify that the culturing steps produce a microbial cell culture having an altered fatty acid profile. Claims 215-284 are methods of use of such microbial culture by virtue of their dependency on claims 189-214. With regard to (b), induction is not a required step, and is not taught to be so in the specification, and no citation to any such

teaching is provided in the Office Action. Expression of the Δ6-desaturase can be constitutive or inducible, as described in the specification. See, for example, page 23, lines 11-27. With regard to (c), the relevant claims as amended recite "extracting said oil with an altered fatty acid profile from the microbial cell culture".

With reference to (d), the Office Action stated that "the phrase 'hybridizes to the complement of the sequence depicted in SEQ ID NO: 1' in claim 275 renders the claims indefinite." The Office Action stated that "[s]ince nucleic acid are no to hybridize to any other nucleic acid sequence under different conditions, the nucleic acid sequence of SEQ ID NO: 1 is expected to hybridize to any nucleic acid sequence. Thus the claim is considered indefinite."

Why this is so is unclear; the Office Action has recognized that the level of skill in the art is high, yet postulates that one of skill in the art is suddenly lobotomized so as to be unable to figure out hybridization conditions specific for a given sequence that is fully disclosed in the instant application. Hybridization using specific probes was routine in the art for over 20 years prior to this invention. Determination of hybridization conditions was and is routine. The Office Action provided no showing why one of skill in the art would choose hybridization conditions under which the probe hybridized to all nucleic acid sequences. That is simply not plausible. One of skill in the art cannot simultaneously possess a high level of skill and no brain.

Furthermore, hybridization is a specific term of art, and requires sufficient complementary base pairing between the hybridizing sequences. A specific sequence would not hybridize to any other sequence. What the Office Action refers to is nonspecific binding. One of skill in the art can readily differentiate between nonspecific binding and hybridization using a simple, standard control sequence.

Nevertheless, claim 214 has been amended to recite that the recombinant nucleic acid "hybridizes to the complement of the sequence depicted in SEQ ID NO: 1 under hybridization conditions suitable for sequencing said complement." Such conditions are specific (sequencing conditions which allowed a primer to hybridize to multiple sequences would not produce usable data), well characterized in the art and readily determinable by one of skill in the art. Primer-based sequencing involves a hybridization step to the template such as the complement of SEQ ID NO:1 as described in the application at page 18 lines 16-28, and working examples of

sequencing are given at page 47 lines 3-7 and lines 17-22 and in Examples 3, 4, 10 and 11, the results of which are shown in the figures and the sequence listings. All parts of the application can provide support for the claims.

Additionally, the application provides explicit support for, and working examples of, PCR based methods of isolating desaturases which include a hybridization step to isolate a desaturase, including solution compositions and hybridization temperatures (see Example 3). Applicants are willing to add claims involving nucleic acids that hybridize under such conditions in response to the next Action.

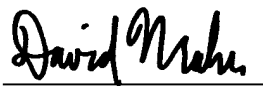
As the claims are clear and definite, withdrawal of the rejection under 35 U.S.C. § 112, second paragraph is respectfully requested.

CONCLUSION

Applicants respectfully request reconsideration of the claims in view of the above amendments and remarks. A notice of allowance is earnestly solicited. If a telephone conference would expedite allowance of this matter, the Examiner is welcome to contact the undersigned at (650) 849-4400.

If an appropriate payment does not accompany or precede this submission, the Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§ 1.16 and 1.17, including any petition for extension of time, or to credit any overpayment, to Deposit Account No. 501189, reference 15611-7032.

Respectfully submitted,

By: 

David Maher
Reg. No. 40,077

Bingham McCutchen LLP
Three Embarcadero Center
San Francisco, California 94111
Telephone: (650) 849-4400
Telefax: (650) 849-4800

ATTACHMENT A

Version with markings to show changes made

IN THE SPECIFICATION

At page 36 lines 23-31:

--The enteral formula can be sterilized and subsequently utilized on a ready-to-feed (RTF) basis or stored in a concentrated liquid or a powder. The powder can be prepared by spray drying the enteral formula prepared as indicated above, and the formula can be reconstituted by rehydrating the concentrate. Adult and infant nutritional formulas are well known in the art and commercially available (e.g., ~~Similac~~SIMILAC® nutritional product, ~~Ensure~~ENSURE® liquid nutritive preparation, ~~Jevity~~JEVITY® liquid nutritive preparation and ~~Alimentum~~ ALIMENTUM® infant formula from Ross Products Division, Abbott Laboratories). An oil or acid of the present invention can be added to any of these formulas in the amounts described below.--

At page 70 line 4:

-- **A. ~~Isomil~~ISOMIL® Soy Formula with Iron.**

--

At page 71 line 12:

-- **B. ~~Isomil~~ISOMIL® DF Soy Formula For Diarrhea.**

--

At page 72 line 19:

-- **C. ~~Isomil~~ISOMIL® SF Sucrose-Free Soy Formula With Iron.**

--

At page 73 lines 19-20:

-- **D. ~~Isomil~~ISOMIL® 20 Soy Formula With Iron Ready to Feed, 20 Cal/fl oz.**

--

At page 74 line 3:

-- **E. ~~Similac~~SIMILAC® Infant Formula**

--

At page 74 lines 24-28:

-- **F. ~~Similac~~SIMILAC® ~~NeoCare~~NEOCARE® Premature Infant Formula With Iron**

Usage: For premature infants' special nutritional needs after hospital discharge. ~~Similac NeoCare~~SIMILAC NEOCARE® infant formula is a nutritionally complete formula developed to provide premature infants with extra calories, protein, vitamins and minerals needed to promote catch-up growth and support development.

--

At page 75 lines 18-19:

-- **G. ~~Similac~~SIMILAC NATURAL CARE® ~~Natural Care~~ Low-Iron Human Milk Fortifier Ready To Use, 24 Cal/fl oz.**

--

At page 76 lines 7-12:

-- **A. ENSURE® Food Supplement**

Usage: ~~ENSURE~~ ENSURE® food supplement is a low-residue liquid food designed primarily as an oral nutritional supplement to be used with or between meals or, in appropriate amounts, as a meal replacement. ~~ENSURE~~ ENSURE® food supplement is lactose- and gluten-free, and is suitable for use in modified diets, including low-cholesterol diets. Although it is primarily an oral supplement, it can be fed by tube.

--

At page 77 lines 2-7:

-- Usage: ENSURE® BARS are complete, balanced nutrition for supplemental use between or with meals. They provide a delicious, nutrient-rich alternative to other snacks. ENSURE® BARS contain <1 g lactose/bar, and Chocolate Fudge Brownie flavor is gluten-free. (Honey Graham Crunch flavor contains gluten.)

--

At page 79 lines 2-8:

-- Usage: ENSURE® HIGH PROTEIN is a concentrate, high-protein liquid food designed for people who require additional calories, protein, vitamins, and minerals in their diets. It can be used as an oral nutritional supplement with or between meals or, in appropriate amounts, as a meal replacement. ENSURE® HIGH PROTEIN is lactose- and gluten-free, and is suitable for use by people recovering from general surgery or hip fractures and by patients at risk for pressure ulcers.

--

At page 80 lines 14-20:

-- The level of fat in ENSURE® HIGH PROTEIN meets American Heart Association (AHA) guidelines. The 6 grams of fat in ENSURE® HIGH PROTEIN represent 24% of the total calories, with 2.6% of the fat being from saturated fatty acids and 7.9% from poly unsaturated fatty acids. These values are within the AHA guidelines of ≤ 30% of total calories from fat, ≤ 1-0% of the calories from saturated fatty acids and ≤ 1-0% of total calories from polyunsaturated fatty acids.

--

At page 80 lines 22-26:

-- ENSURE® HIGH PROTEIN contains a combination of maltodextrin and sucrose. The mild sweetness and flavor variety (vanilla supreme, chocolate royal, wild berry, and banana), plus VARI-FLAVORS® Flavor Pacs food flavors in pecan, cherry, strawberry, lemon, and orange, help to prevent flavor fatigue and aid in patient compliance.

--

At page 81 lines 6-10:

-- Usage: ENSURE® LIGHT is a low-fat liquid food designed for use as an oral nutritional supplement with or between meals. ENSURE® LIGHT is lactose- and gluten-free, and is suitable for use in modified diets, including low-cholesterol diets.

--

At page 82 lines 14-19:

-- The level of fat in ENSURE® LIGHT meets American Heart Association (AHA) guidelines. The 3 grams of fat in ENSURE® LIGHT represent 13.5% of the total calories, with 1.4% of the fat being from saturated fatty acids and 2.6% from polyunsaturated fatty acids. These values are within the AHA guidelines of $\leq$ 30% of total calories from fat, $\leq$ 1-0% of the calories from saturated fatty acids and $\leq$ 1-0% of total calories from polyunsaturated fatty acids.

--

At page 82 lines 21-25:

-- ENSURE® LIGHT contains a combination of maltodextrin and sucrose. The chocolate flavor contains corn syrup as well. The mild sweetness and flavor variety (French vanilla, chocolate supreme, strawberry swirl), plus VARI-FLAVORS® Flavor Pacs food flavors in pecan, cherry, strawberry, lemon, and 25 orange, help to prevent flavor fatigue and aid in patient compliance.

--

At page 83 lines 6-7:

-- An 8-fl-oz serving of ENSURE® LIGHT provides at least 25% of the RDIs for 24 key vitamins and minerals.

--

At page 83 lines 11-17:

-- **E. ENSURE PLUS® Liquid Nutritive Preparation**

Usage: ENSURE PLUS® liquid nutritive preparation is a high-calorie, low-residue liquid food for use when extra calories and nutrients, but a normal concentration of protein, are needed. It is designed primarily as an oral nutritional supplement to be used with or between meals or, in

appropriate amounts, as a meal replacement. ENSURE PLUS® liquid nutritive preparation is lactose- and gluten-free. Although it is primarily an oral nutritional supplement, it can be fed by tube.

--

At page 84 lines 18-22:

-- ENSURE PLUS® liquid nutritive preparation contains a combination of maltodextrin and sucrose. The mild sweetness and flavor variety (vanilla, chocolate, strawberry, coffee, butter pecan, and eggnog), plus VARI-FLAVORS® Flavor Pacs food flavors in pecan, cherry, strawberry, lemon, and orange, help to prevent flavor fatigue and aid in patient compliance.

--

At page 85 lines 4-5:

-- An 8-fl-oz serving of ENSURE PLUS® liquid nutritive preparation provides at least 15% of the RDIs for 25 key Vitamins and minerals.

--

At page 85 lines 10-15:

-- **F. ENSURE PLUS® HN Liquid Nutritive Preparation**

Usage: ENSURE PLUS® HN liquid nutritive preparation is a nutritionally complete high-calorie, high-nitrogen liquid food designed for people with higher calorie and protein needs or limited volume tolerance. It may be used for oral supplementation or for total nutritional support by tube. ENSURE PLUS® HN liquid nutritive preparation is lactose- and gluten-free.

--

At page 86 lines 13-16:

-- Usage: ENSURE® POWDER (reconstituted with water) is a low-residue liquid food designed primarily as an oral nutritional supplement to be used with or between meals. ENSURE® POWDER is lactose- and gluten-free, and is suitable for use in modified diets, including low-cholesterol diets.

--

At page 87 lines 19-22:

-- ENSURE® POWDER contains a combination of corn syrup, maltodextrin, and sucrose. The mild sweetness of ENSURE® POWDER , plus VARI-FLAVORS® Flavor Pacs food flavors in pecan, cherry, strawberry, lemon, and orange, helps to prevent flavor fatigue and aid in patient compliance.

--

At page 88 lines 2-5:

-- Usage: ENSURE® PUDDING is a nutrient-dense supplement providing balanced nutrition in a nonliquid form to be used with or between meals. It is appropriate for consistency-modified diets (e.g., soft, pureed, or full liquid) or for people with swallowing impairments. ENSURE® PUDDING is gluten-free.

--

At page 89 lines 5-8:

-- ENSURE® PUDDING contains a combination of sucrose and modified food starch. The mild sweetness and flavor variety (vanilla, chocolate, butterscotch, and tapioca) help prevent flavor fatigue. The product contains 9.2 grams of lactose per serving.

--

At page 89 lines 18-25:

-- **I. ENSURE® WITH FIBER**

Usage: ENSURE® WITH FIBER is a fiber-containing, nutritionally complete liquid food designed for people who can benefit from increased dietary fiber and nutrients. ENSURE® WITH FIBER is suitable for people who do not require a low-residue diet. It can be fed orally or by tube, and can be used as a nutritional supplement to a regular diet or, in appropriate amounts, as a meal replacement. ENSURE® WITH FIBER is lactose- and gluten-free, and is suitable for use in modified diets, including low-cholesterol diets.

--

At page 91 lines 7-13:

-- The level of fat in ENSURE® WITH FIBER meets American Heart Association (AHA) guidelines. The 6 grams of fat in ENSURE® WITH FIBER represent 22% of the total calories, with 2.01% of the fat being from saturated fatty acids and 6.7% from polyunsaturated fatty acids. These values are within the AHA guidelines of ≤ 30% of total calories from fat, ≤ 10% of the calories from saturated fatty acids and ≤ 10% of total calories from polyunsaturated fatty acids.

--

At page 91 lines 15-18:

-- ENSURE® WITH FIBER contains a combination of maltodextrin and sucrose. The mild sweetness and flavor variety (vanilla, chocolate, and butter pecan), plus VARI-FLAVORS® Flavor Pacs food flavors in pecan, cherry, strawberry, lemon, and orange, help to prevent flavor fatigue and aid in patient compliance.

--

At page 92 lines 3-5:

-- The fiber blend used in ENSURE® WITH FIBER consists of oat fiber and soy polysaccharide. This blend results in approximately 4 grams of total dietary fiber per 8-fl-oz can. The ratio of insoluble to soluble fiber is 95:5.

--

At page 92 lines 9-14:

-- **J. OXEPA® ~~Oxepa™~~ Nutritional Product**

~~Oxepa~~OXEPA® is a low-carbohydrate, calorically dense enteral nutritional product designed for the dietary management of patients with or at risk for ARDS. It has a unique combination of ingredients, including a patented oil blend containing eicosapentaenoic acid (EPA from fish oil), γ-linolenic acid (GLA from borage oil), and elevated antioxidant levels.

--

At page 92 line 18:

--

- The distribution of Calories in ~~Oxepa~~OXEPA® nutritional product is shown in Table 7.

--

The table at page 92 line 19:

--

Table 7. Caloric Distribution of ~~Oxepa~~OXEPA® Nutritional Product			
	per 8 fl oz.	**per liter**	**% of Cal**
Calories	355	1,500	---
Fat (g)	22.2	93.7	55.2
Carbohydrate (g)	25	105.5	28.1
Protein (g)	14.8	62.5	16.7
Water (g)	186	785	---

--

At page 92 line 21:

--

- ~~Oxepa~~OXEPA® nutritional product contains 22.2 g of fat per 8-fl oz serving (93.7 g/L).

--

At page 92 lines 22-24:

--

- The fat source is a oil blend of 31.8% canola oil, 25% medium-chain triglycerides (MCTs), 20% borage oil, 20% fish oil, and 3.2 % soy lecithin. The typical fatty acid profile of ~~Oxepa~~OXEPA® nutritional product is shown in Table 8.

--

At page 93 lines 1-2:

--

- ~~Oxepa~~OXEPA® nutritional product provides a balanced amount of polyunsaturated, monounsaturated, and saturated fatty acids, as shown in Table 10.

--

At page 93 lines 6-7:

-- The various fatty acid components of ~~Oxepa™~~OXEPA®- nutritional product can be substituted and/or supplemented with the PUFAs of this invention.

--

The table at page 93 line 9:

--

Table 9. Fat Profile of ~~Oxepa~~OXEPA® Nutritional Product	
% of total calories from fat	55.2
Polyunsaturated fatty acids	31.44 g/L
Monounsaturated fatty acids	25.53 g/L
Saturated fatty acids	32.38 g/L
n-6 to n-3 ratio	1.75:1
Cholesterol	9.49 mg/8 fl oz 40.1 mg/L

--

At page 94 lines 6-10:

--

- The high-fat and low-carbohydrate content of ~~Oxepa~~OXEPA® nutritional product is designed to minimize carbon dioxide (CO_2) production. High CO_2 levels can complicate weaning in ventilator-dependent patients. The low level of carbohydrate also may be useful for those patients who have developed stress-induced hyperglycemia.

--

At page 94 line 11:

--

- ~~Oxepa~~OXEPA® nutritional product is lactose-free.

--

At page 94 lines 12-20:

-- Dietary carbohydrate, the amino acids from protein, and the glycerol moiety of fats can be converted to glucose within the body. Throughout this process, the carbohydrate requirements of glucose-dependent tissues (such as the central nervous system and red blood cells) are met. However, a diet free of carbohydrates can lead to ketosis, excessive catabolism of tissue protein, and loss of fluid and electrolytes. These effects can be prevented by daily ingestion of 50 to 100 g of digestible carbohydrate, if caloric intake is adequate. The carbohydrate level in ~~Oxepa~~OXEPA® nutritional product is also sufficient to minimize gluconeogenesis, if energy needs are being met.

--

At page 94 line 22:

--

- ~~Oxepa~~OXEPA® nutritional product contains 14.8 g of protein per 8-fl-oz serving (62.5 g/L).

--

At page 94 lines 24-28:

--

- ~~Oxepa~~OXEPA® nutritional product provides enough protein to promote anabolism and the maintenance of lean body mass without precipitating respiratory problems. High protein intakes are a concern in patients with respiratory insufficiency.

Although protein has little effect on CO_2 production, a high protein diet will increase ventilatory drive.

--

At page 95 lines 1-2:

--

- The protein sources of ~~Oxepa~~OXEPA® nutritional product are 86.8% sodium caseinate and 13.2% calcium caseinate.

--

At page 95 lines 3-5:

--

- As demonstrated in Table 11, the amino acid profile of the protein system in ~~Oxepa~~OXEPA® nutritional product meets or surpasses the standard for high quality protein set by the National Academy of Sciences.

--

At page 95 line 6:

--

- ~~Oxepa~~OXEPA® nutritional product is gluten-free.

--

IN THE CLAIMS

189. (Amended) A method for producing a microbial cell culture with an altered fatty acid profile comprising:

culturing a microbial cell comprising a recombinant nucleic acid comprising the sequence depicted in SEQ ID NO: 1 to produce the microbial cell culture, said nucleic acid operably

linked to transcription and translation control signals functional in said cell, wherein a polypeptide encoded by said nucleic acid is expressed in sufficient amount in said ~~cell~~ culture to alter the fatty acid profile ~~of said cell~~.

193. (Amended) A method for producing a microbial cell culture with an altered fatty acid profile comprising:

culturing a microbial cell comprising a recombinant nucleic acid with at least ~~50%~~ 80% homology to the sequence depicted in SEQ ID NO: 1 to produce the microbial cell culture, said nucleic acid operably linked to transcription and translation control signals functional in said cell, wherein a polypeptide encoded by said nucleic acid forms a monounsaturated bond between carbons 5 and 6 of a fatty acid as numbered from a carboxy terminus thereof, wherein said polypeptide is expressed in sufficient amount in said ~~cell~~ culture to alter the fatty acid profile ~~of said cell~~.

201. (Amended) A method for producing a microbial cell culture with an altered fatty acid profile comprising:

culturing a microbial cell comprising a recombinant nucleic acid operably linked to transcription and translation control signals functional in said cell to produce the microbial cell culture, wherein said nucleic acid is a deletion mutant of the nucleic acid depicted in SEQ ID NO: 1, wherein a polypeptide encoded by said nucleic acid forms a monounsaturated bond between carbons 5 and 6 of a fatty acid as numbered from a carboxy terminus thereof, wherein said polypeptide is expressed in sufficient amount in said ~~cell~~ culture to alter the fatty acid profile ~~of said cell~~.

205. (Amended) A method for producing a microbial cell culture with an altered fatty acid profile comprising:

culturing a recombinant microbial cell comprising a polypeptide comprising the amino acid sequence depicted in SEQ ID NO:2 to produce the microbial cell culture, wherein said polypeptide is expressed in sufficient amount in said ~~cell~~ culture to alter the fatty acid profile ~~of said cell~~.

208. (Amended) A method for producing a microbial cell culture with an altered fatty acid profile comprising:

culturing a recombinant microbial cell comprising a polypeptide with at least ~~60%~~ 80% homology to the sequence depicted in SEQ ID NO: 2 to produce the microbial cell culture, wherein said polypeptide forms a monounsaturated bond between carbons 5 and 6 of a fatty acid as numbered from a carboxy terminus thereof, wherein said polypeptide is expressed in sufficient amount in said ~~cell~~ culture to alter the fatty acid profile ~~of said cell~~.

214. (Amended) A method for producing a microbial cell culture with an altered fatty acid profile comprising:

culturing a microbial cell comprising a recombinant nucleic acid to produce the microbial cell culture, wherein said nucleic acid ~~that~~ hybridizes to the complement of the sequence depicted in SEQ ID NO: 1 under hybridization conditions suitable for sequencing said complement, said nucleic acid operably linked to transcription and translation control signals functional in said cell, wherein a polypeptide encoded by said nucleic acid forms a monounsaturated bond between carbons 5 and 6 of a fatty acid as numbered from a carboxy terminus thereof, wherein said polypeptide is expressed in sufficient amount in said ~~cell~~ culture to alter the fatty acid profile ~~of said cell~~.

215. (Amended) A method for producing oil with an altered fatty acid profile comprising extracting said oil with an altered fatty acid profile from the microbial cell culture produced according to the method of claim 189.

225. (Amended) A method for producing oil with an altered fatty acid profile comprising extracting said oil with an altered fatty acid profile from the microbial cell culture produced according to the method of claim 193.

235. (Amended) A method for producing oil with an altered fatty acid profile comprising extracting said oil with an altered fatty acid profile from the microbial cell culture produced according to the method of claim 201.

245. (Amended) A method for producing oil with an altered fatty acid profile comprising extracting said oil with an altered fatty acid profile from the microbial cell culture produced according to the method of claim 202.

255. (Amended) A method for producing oil with an altered fatty acid profile comprising extracting said oil with an altered fatty acid profile from the microbial cell culture produced according to the method of claim 205.

265. (Amended) A method for producing oil with an altered fatty acid profile comprising extracting said oil with an altered fatty acid profile from the microbial cell culture produced according to the method of claim 208.

275. (Amended) A method for producing oil with an altered fatty acid profile comprising extracting said oil with an altered fatty acid profile from the microbial cell culture produced according to the method of claim 214.